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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/339,818	06/25/1999	MARK E. DAVIS	038134-50010	3090
28120	7590	06/17/2004	EXAMINER	
ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			CRANE, LAWRENCE E	
			ART UNIT	PAPER NUMBER

1623

DATE MAILED: 06/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/339,818	Applicant(s) DAVIS ET AL.	
	Examiner L. E. Crane	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on November 10, 2003 (amdt).
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,6-10,18,24-26,30-34,44,46 and 58-64 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,6-10,18,24-26,30-34,44,46 and 58-64 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 May 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>February 19, 2002</u> . | 6) <input type="checkbox"/> Other: _____ |

No claims have been cancelled, claims **6, 9-10, 24 and 30-32** have been amended, no further amendments to the disclosure have been submitted, and no additional new claims have been added as per the amendment filed November 10, 2003. No additional Information Disclosure Statements (IDSs) have been submitted as of the mailing date of this Office action.

Claims **1-3, 6-10, 18, 24-26, 30-34, 44, 46 and 58-64** remain in the case.

Applicant has requested examiner to reconsider the "Pun (Hwang) declaration." Because the rejection over "Kosak '736" has been withdrawn, consideration of the noted declaration is deemed to have been rendered moot.

Claims **1-3, 6-10, 18, 24-26, 30-34, 44, 46 and 58-64** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims have not met the written description standard of *Regents of the University of California v. Eli Lilly* (119F.3d 1559 at 1568; 43 USPQ2d 1398 at 1406 (Fed. Cir 1997)): see MPEP §2163 at page 2100 et seq. Applicant is requested to note that examiner has carefully reviewed the examples of the disclosure, particularly Examples 5, 6, 7, 8, 9, 10, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23 and 24, and has noted in particular the repeated allegations similar to that found in Example 5 at page 31 which is quoted in part as follows: "[GPC] Fractions were analyzed by GPC and appropriate fractions were lyophilized to yield ... as a ... solid." Examiner found on reference to NMR (Ex. 17) but has failed to find any analytical data establishing molecular weight, elemental composition or mass spectra before and after the selection of the "appropriate fractions" in any synthesis of any water soluble cyclodextrin within the noted Examples. Examiner has also failed to find any examples wherein a complete detailed description of any single GPC purification protocol, or GPC analysis protocol, or both, has been presented. Because complete details of the GPC separation/analysis processes are necessarily critical to isolation and identification of the instant claimed products, the instant disclosure is deemed lack an adequate written description, i.e. to be incomplete, without same. Because no other analytical data has been presented as

part of the synthesis of any cyclodextrin oligomer/polymer, there are no factual bases presently to be found within the disclosure which would permit the ordinary practitioner to otherwise infer the requisite details of the GPC protocols in the course of routine experimentation directed to reproducing the isolation of the particular products claimed herein. Similar criticism applies to examples like Example 19 at pages 45-46 wherein "lyophilization" is cited as the purification procedure, but the particular details of how applicant practiced same are not provided.

Applicant's arguments filed November 10, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant argues that the instant rejection is inappropriate "because the purification details are not disclosed in exquisite detail." Examiner has noted that the end of each and every one of the experimental procedures applicant has not provided analytical data even when it is clear that such data was available (reference to an NMR in one case). As the quoted "Written Description Guidelines" note, applicant's burden is to provide a "sufficient description" which in the instant case has not been provided where it counts most, in the analytical portion of the experimental procedures. The missing data for even a single example would prove that applicant had possession.

Applicant then argues that the missing data could be supplied by the ordinary practitioner, but this argument fails because the ordinary practitioner has no single set of physical reference data to compare with; e.g. water solubility, melting point, NMR, Mass Spectra or other molecular weight range determination, GPC curve with conditions, etc.

Because applicant has provided detailed quantities of reactants, and some reaction conditions, and has referred to analytical data, examiner assumes that such data is available. In the interest of making the record complete so that the ordinary practitioner can practice at least one procedure without undue experimentation, examiner will accept the following submission as a means to overcome the instant grounds of rejection: a declaration under 37 C.F.R. §1.132 which provides complete analytical data and details of how one claimed CD-containing oligomeric compound was made and identified, wherein "complete" means all presently disclosed data, plus i) reaction time, ii) reaction temperature(s), iii) product NMR, iv) product GPC trace with

complete data on the specific GPC conditions applied, and v) product Mass Spectra or other valid molecular weight range determination of said product. Such a submission will not be considered to be new matter.

Claims 1-2, 7-10, 18, 24-26, 31-34, 44, 46 and 58-64 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In each of claims 1-2, 7-10, 18, 24-26, 31-34, 44, 46 and 58-64 functional terminology is present which describes chemical functionalities of a “cyclodextrin”-containing species, a “comonomer A,” and the like, but fails to further define same in sufficient detail to permit one of ordinary skill to be able to determine the particular chemical species being referred to; a metes and bounds problem. For example, in claim 1 the terms “water soluble” and “linear” modify the term “cyclodextrin copolymer,” but fail to define what particular chemical functional groups and chemical linkages are present between the cyclodextrin and comonomer A. The chemical structure or structures of “comonomer A” is/are not defined in any way in claim 1. In claim 24 precursors to the polymer are defined as being disubstituted (“cyclodextrin comonomer precursor”) and “comonomer A” is described as being “capable of displacing said leaving groups to form a linear cyclodextrin copolymer having repeating groups” Claim 25 defines the cyclodextrin reactant, but is incomplete for failure to define structural identity of the chemical crosslinkers (comonomer A) which are needed to produce the product. Claim 31 adds a “ligand” attachment step, but fails to define a chemical reagent for effecting such a step. Claim 32 narrows the subject matter slightly, but fails to define what “aminating reagent” or “reagents” are converting the di-iodocyclodextrins of claim 25 to “diamino” analogues. Claim 58 is directed to reacting a “cyclodextrin derivative modified to bear one reactive site at each of exactly two positions,” suggesting that either valence rules are being violated, or that applicant has not clearly described the subject matter. Similarly, claim 58 is directed to a “linker” which has “exactly two reactive moieties capable of forming a covalent bound with the reactive the reactive sites [of the cyclodextrin derivative] under polymerization conditions,” but has failed to define the chemical identity or identities of the “reactive moieties” or the particular “polymerization conditions” being referred to. See also claim 61. See also compound claims 59, 60 and 62-64 which have the same or similar problems following from reliance on functional terminology.

Applicant's arguments filed November 10, 2003 have been fully considered but they are not deemed to be persuasive.

As applicant notes in the response of November 10, 2003, the question is whether the claims "set out and circumscribe a particular subject matter with a reasonable degree of particularity." (emphasis added). In light of the instant newly cited prior art (art rejection below) kindly supplied previously by applicant, it is evident that applicant's disclosure fails to describe the work of the '194 reference, but that the generic claims listed in the rejection below read on said reference. Therefore, examiner suggests that applicant should now seek to avoid said reference by limiting the instant claims to a much less generic, and much more structurally specific, scope. In so doing, examiner suggests the possibility that the instant grounds of rejection could also be avoided.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

Claims 1-3, 7, 24-26, 32-33, 58-60 and 62-64 are rejected under 35 U.S.C. §102 (b) as being anticipated by **Toppan Printing Co. '194** (PTO-1449 ref. **BM**).

Applicant is referred to the noted reference wherein a large number of exemplifications disclose linear polymers of α -, β - and γ -cyclodextrins wherein cyclodextrin intermediates (some of which are very similar or identical to those disclosed herein) are converted into various enzyme-degradable polymers with urethane, urea, unsaturated ester, ester, carbonate, amide and sulfone linkages between the cyclodextrin units. The cyclodextrin polymer products are required to be linear by the protecting group strategy applied or by using bridged cyclodextrin precursors. See examples illustrated by oligomeric structures at pages 18-19, 27-29, 31-32 and 37-39. Note also that the proposed structures (only primary hydroxyl shown to react) do not

exclude the possibility that the actual products produced result from reaction with primary **and/or** secondary cyclodextrin hydroxyls; e.g. boronic acids and aldehydes are both notoriously well known to form stable cyclic compounds with vicinal dihydroxy compounds (glycols), a functionality found only on the secondary (open) side of cyclodextrins. In addition, at page 26, lines 14-15, reference is made to "low-molecular weight oligomers" ... "extracted with hot ethanol," a class of oligomeric compounds which are presumed to have some water solubility. And lastly, at page 8 of the '194 reference, applicant is referred to the conversion of compound "[6]" into compound "[B]" at lines 35-45 of column 2 and associated explanatory text as anticipating the cited method of making claims. Therefore, the cited reference is deemed anticipate both of the generic structures of instant claim 1 and methods of making same.

Applicant's arguments with respect to claims **1-3, 7, 24-26, 32-33, 58-60 and 62-64** have been considered but are deemed to be moot in view of the new grounds of rejection.

Claims **6, 8-10, 18, 30-31, 34, 44, 46 and 61** would be allowable if rewritten or amended to overcome the rejection under 35 U.S.C. 112.

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 703-872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

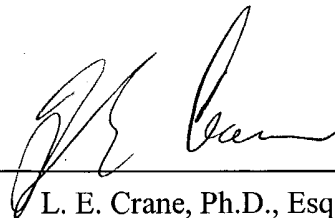
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at **571-272-0661**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

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LECrane:lec
06/16/2004

A handwritten signature in black ink, appearing to read "L. E. Crane", is positioned above a horizontal line.

L. E. Crane, Ph.D., Esq.
Primary Patent Examiner
Technology Center 1600